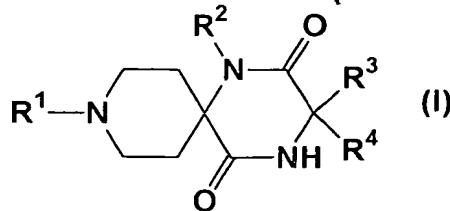


CLAIMS

1. A compound represented by formula (I),



wherein R¹ represents (1) ring 1, or (2) C1-8 alkyl, C2-4 alkenyl or C2-4 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(i): (a) -OR⁵, (b) -COR⁶, (c) -NR⁷R⁸, (d) -CONR⁹R¹⁰, (e) -NR¹¹COR¹², (f) -NR¹³SO₂R¹⁴, (g) ring 1, (h) =NR¹⁵, (i) =NOR¹⁶,

R⁵-R¹³, R¹⁵ and R¹⁶ each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 1, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from ring 1 and -O-ring 1,

R¹⁴ represents C1-4 alkyl or ring 1,

ring 1 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 1 may be substituted with 1-5 substituents selected from (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) ring 2, (7) -OR¹⁷, (8) -SR¹⁸, (9) -NR¹⁹R²⁰, (10) -COR²¹, (11) -COOR²², (12) -CONR²³R²⁴, (13) -NR²⁵COR²⁶, (14) -SO₂NR²⁷R²⁸, (15) -NR²⁹SO₂R³⁰, (16) -N(SO₂R³¹)₂, (17) oxo, and (18) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(e): (a) halogen, (b) ring 2, (c) -OR³², (d) -NR³³COR³⁴, (e) =NOR³⁵,

R¹⁷-R²⁹ and R³²-R³⁵ each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 2, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(f): (a) ring 2, (b) -OR³⁶, (c) -COOR³⁷, (d) -NR³⁸R³⁹, (e) halogen, (f) =NR⁴⁰,

R³⁰ and R³¹ each represents C1-4 alkyl,

R³⁶-R⁴⁰ each represents hydrogen or C1-4 alkyl optionally substituted with hydroxyl,

ring 2 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 2 may be substituted with 1-5 substituents selected from (1) C1-8 alkyl, (2) halogen, (3) -OCF₃, (4) cyano, (5) ring 3, (6) -OR⁴¹, (7) -NR⁴²R⁴³, (8) -COR⁴⁴, (9) -COOR⁴⁵, (10) -CONR⁴⁶R⁴⁷, (11) -NR⁴⁸COR⁴⁹, (12) -SO₂NR⁵⁰R⁵¹, (13) -NR⁵²SO₂R⁵³, and (14) -C(NH₂)=NR⁵⁴,

R⁴¹-R⁵² and R⁵⁴ each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 3, (6) -OR⁵⁵, or (7) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(d): (a) ring 3, (b) -OR⁵⁶, (c) -COOR⁵⁷, (d) -NR⁵⁸R⁵⁹,

R⁵³ represents C1-8 alkyl,

R⁵⁵-R⁵⁹ each represents hydrogen or C1-4 alkyl,

ring 3 represents (1) C3-8 mono-carbocyclic aryl which may be partially or fully saturated, or (2) 3-8 membered mono-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 3 may be substituted with 1-3 of =O or =S,

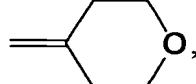
R² represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 4, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(i): (a) hydrogen, (b) -OR⁶⁰, (c) -NR⁶¹R⁶², (d) -CONR⁶³R⁶⁴, (e) -NR⁶⁵COR⁶⁶, (f) -NR⁶⁷SO₂R⁶⁸, (g) NR⁶⁹COOR⁷⁰, (h) ring 4, (i) cyano,

R⁶⁰-R⁶⁷ and R⁶⁹ each represents hydrogen, C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,

R⁶⁸ and R⁷⁰ each represents C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl,

ring 4 represents phenyl, pyridinyl, or C3-8 cycloalkyl,

ring 4 may be substituted with 1-5 of C1-4 alkyl,

R³ and R⁴ together with a carbon atom to which they are attached, form C3-8 cycloalkyl, or R³ and R⁴ each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(c): (a) ring 5, (b) hydroxyl, (c) 

ring 5 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 5 may be substituted with 1-5 of -OR⁷¹, C1-4 alkyl or oxo,

R⁷¹ represents hydrogen or C1-4 alkyl,

a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

2. The compound according to claim 1, which is selected from the group consisting of

- (1) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonyl-2-chlorophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (2) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-(5-oxo-4,5-dihydro-1,2,4-thiadiazol-3-yl)phenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (3) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(4-(2-methoxyethylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (4) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-methylpropyl)-9-(4-(4-methylsulfonylaminoo-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (5) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(pyrrolidin-1-yl)carbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (6) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(2-methoxy-4-methylsulfonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (7) (3S)-1-butyl-2,5-dioxo-3-(2-methylpropyl)-9-(4-(2-methoxy-4-methylsulfonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (8) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylaminophenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (9) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylaminoo-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (10) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(2-(4-methylaminocarbonylphenoxy)ethyl)-1,4,9-triazaspiro[5.5]undecane,
- (11) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(5-(4-methylaminocarbonylphenoxy)pentyl)-1,4,9-triazaspiro[5.5]undecane,
- (12) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane,
- (13) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclohexen-4-yl)methyl)-9-(4-(4-methylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (14) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylsulfonylaminophenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane, and
- (15) (3R)-1-pentyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane.

3. The compound according to claim 1, which is selected from the group consisting of

- (1) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-cyclopropylmethylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (2) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (3) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (4) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (5) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-(N,N-dimethylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (6) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (7) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2,6-dimethylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (8) (3R)-1-pentyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (9) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (10) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-cyclopropylmethylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (11) (3R)-1-propyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-dimethylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (12) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cycloheptylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (13) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclopentylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (14) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclopentylmethyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (15) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-cyclopropylmethylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (16) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-methylaminocarbonyl-2-methoxyphenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
- (17) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(18) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)aminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(19) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2,2-dimethylpropylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(20) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylcarbonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(21) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(22) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylcarbonylamino-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(23) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclopenten-4-yl)methyl)-9-(4-(4-carboxy-2-methylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(24) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclopenten-4-yl)methyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(25) (3R)-1-(2-butynyl)-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane,

(26) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(1-(4-(4-methylaminocarbonylphenoxy)phenyl)ethyl)-1,4,9-triazaspiro[5.5]undecane, and

(27) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(1-(4-(4-carboxyphenoxy)phenyl)ethyl)-1,4,9-triazaspiro[5.5]undecane.

4. The compound according to claim 1, wherein R¹ is C1-8 alkyl, C2-4 alkenyl, or C2-4 alkynyl substituted with -COR⁶, =NR¹⁵, or =NOR¹⁶, in which R⁶, R¹⁵ and R¹⁶ have the same meanings as defined in claim 1.

5. The compound according to claim 1, wherein at least one of substituents of ring 1 in R¹ is -COR¹², oxo, or =NOR³⁵, in which R¹² and R³⁵ have the same meanings as defined in claim 1.

6. The compound according to claim 1, wherein at least one of substituents of ring 2 in R¹ is -COR⁴⁴ or -C(NH₂)=NOR⁵⁴, in which R⁴⁴ and R⁵⁴ have the same meanings as defined in claim 1.

7. The compound according to claim 1, wherein at least one of substituents of ring 3 in R¹ is =O or =S.

8. A pharmaceutical composition which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

9. A regulator of a chemokine/chemokine receptor, which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

10. The regulator of a chemokine/chemokine receptor according to claim 9, which is a CCR5 antagonist.

11. A pharmaceutical composition for prevention and/or treatment for inflammatory diseases, immunologic diseases, human immunodeficiency virus, allergic diseases, ischemia-reperfusion injury, acute respiratory distress syndrome, shock accompanied by bacterial infection, diabetes mellitus, or metastasis, which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt.

12. A method for antagonizing CCR5 in a mammal, which comprises administering to a mammal an effective amount of the compound of formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

13. Use of the compound of formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof for the manufacture of a CCR5 antagonist.